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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ROCHE MOLECULAR SYSTEMS INC
PATENT LAW DEPARTMENT
1145 ATLANTIC AVENUE
ALAMEDA, CA 94501

EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,649	SMITH ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-16,20-32,36-44 and 48-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-16,20-32,36-44 and 48-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *803; 603* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed June 30, 2003. Currently, claims 1-4, 8-16, 20-32, 36-44, 48-68 are pending.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

1. Any objections and rejections not reiterated below are hereby withdrawn in view of the amendments to the claims or applicant's arguments.

2. This action contains new grounds of rejection necessitated by amendment.

Priority

3. This application claims priority to provisional application 60/198,336, filed April 18, 2000.

As provided in the March 1, 2003 O.G. Notice: "an incorporation-by-reference statement added after the filing date of an application is not permitted because no new matter can be added to an application after its filing date. See 35 U.S.C. 132(a). If an incorporation-by-reference statement is included in an amendment to the specification to add a benefit claim after the filing date of the application, the amendment would not be proper. When a benefit claim is submitted after the filing of an application, the reference to the prior application cannot include an incorporation-by-reference statement of the prior application. See Dart Industries v. Banner, 636 F.2d 6 4, 207 USPQ 273 (C.A.D.C. 190).

The instant amendments to the specification are therefore objected to as new matter because the incorporation by reference is inappropriate.

Maintained Rejections

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 8-13, 20-29, 36-41, 48-52, Newly added Claims 53, 57, 61, 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for reverse transcribing an RNA using a mutant DNA polymerase characterized in that in its native form said DNA polymerase comprises SEQ ID NO: 3, and at position 4 of said amino acid sequence the amino cid is other than E,A,G or P, does not reasonably provide enablement for any mutant polymerase of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working

examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn methods for reverse transcribing an RNA using a mutant DNA polymerase wherein the DNA polymerase is characterized in that "in its native form the DNA polymerase comprises amino acid sequence of SEQ ID NO: 1." SEQ ID NO: 1 is LeuXaaXaaXaaXaaXaaXaaXaaXaaXaaGlu where Xaa at positions 2 is either S or A; position 5 is either L or I; and positions 6, 7, 8, 9, 10 are any amino acid, Xaa at position 4 is not Glu, A, G or P.

The specification teaches six more specific genus within the very broad genus of SEQ ID NO: 1. These genus are identified by SEQ ID NO: 2-7. The specification, in Table 1, provides an alignment of "the critical motif" of DNA polymerases. The Table highlights position 4. The specification teaches that each of the mutant polymerases had been previously disclosed. The "critical motif identifies a particular functional region within the polymerase domain of the enzyme, and identifies an amino acid within the motif that is critical to the function" (page 12, lines 35-38). The specification asserts that the structural relatedness of DNA polymerases and the presence of conserved functional domains is well known. The specification explains that "additional substitution mutation in position 3 of the critical motifs identified as SEQ ID NO: 1-7 may provide additional benefits" (page 14, lines 14-16). The specification provides a single example of the effects on Mg-activated reverse transcription efficiency of each possible mutation at this site in one widely used thermostable DNA polymerase, Thermus thermophilus DNA polymerase. In Example 1, a "series of 19 mutant DNA polymerases were

constructed from "native" Termus thermophilus (Tth) DNA polymerase representing all possible mutations in the critical amino acid (page 18). The results of the reaction efficiencies are provided for each of the possible mutations at position 4 (page 24).

As claimed, the independent claim, namely Claims 1, 13, 29, 44, encompasses any DNA polymerase which minimally contains a Leu amino acid at position 1; a S or A at position 2; a L or I at position 5 and Glu at position 11. The specification teaches a single example of a very defined structure with a single variable position, namely position 4. The claims are drawn much broader to read on a large genus of sequences which have not been defined by the specification with respect to their reaction efficiencies. The specification teaches that position 683 is the critical amino acid for Taq polymerase. As seen in the alignment provided in Table 1, the identified critical motif contains many conserved positions among several species, however, not complete conservation between all species. It is unpredictable which of the additional positions within the "critical motif" would affect the reverse transcription properties of the polymerase. The specification has demonstrated one specific example, namely SEQ ID NO: 3 with each of the variations between the possible mutants. Given the teachings from this example, it is unpredictable how additional mutations or variations within SEQ ID NO: 3 will affect the reaction efficiencies of alternative polymerases. In the broadest claim, SEQ ID NO: 1 identifies only 5 of 11 positions within the polymerase. This very broad definition of structure does not provide guidance to the skilled artisan how to use the entire scope of the claims. Absent undue trial and error experimentation, to determine whether each of the possible alternatives have the DNA polymerase activity,

the skilled artisan would be unable to use the invention as broadly as claimed. There are 20 possible alternatives for each of the 6 undefined positions within SEQ ID NO: 1. Given all of the possible permutations encompassed within the claim, the claim encompasses 4,096,000,000 different amino acid sequences. While one could conduct additional experimentation to determine whether, e.g. each of these permutations might have DNA polymerase activity, the outcome of such research cannot be predicted and such further research and experimentation are both unpredictable and undue.

Response to Arguments

The response traverses the rejection. The response asserts that "one of only ordinary skill in the art can easily recognize and use any species within the genus of thermostable DNA polymerase enzymes recited by the claims" (Page 17, para 1). The response further argues, that any experimentation required to practice the full scope of the invention is routine rather than undue (page 18). This argument has been reviewed but is not convincing because although the practice of detecting the requisite motif in a DNA polymerase and the introduction of single amino acid substitutions are within the level of skill of the artisan, the effect of single amino acid substitutions on the polymerases ability to reverse transcribe RNA is unpredictable given the disclosure in the specification. It is unpredictable the effects of various substitutions and mutations within the polymerase. It is unclear whether the polymerase may tolerate mutations at each of the variable sites. It is clear based upon the data shown in the specification that changes in amino acids, at position 4, for example, affect the DNA polymerase by either enhancing or inhibiting the efficiency of the reaction. It is unpredictable whether

additional mutations within the "critical motif" will be unable to polymerize and thus would be unable to reverse transcribe RNA. While one could perform the experimentation of determining whether the substitutions within the critical motif alter the ability of reverse transcription, the experimentation is unpredictable and undue. It is unpredictable which substitutions would have a negative or positive or null effect on the reverse transcription prior to testing each possible combination. Moreover, testing each possible combination, would amount to undue experimentation.

The response asserts that the art would confirm that the enzyme is a thermostable DNA polymerase enzyme by comparing the primary structures of the thermostable DNA polymerases to the primary structure of known thermostable DNA polymerase enzymes. This argument has been thoroughly reviewed, but is not found persuasive because there is no discussion of the primary structure required for a DNA polymerase enzyme to perform reverse transcriptase. Thus, the ordinary artisan would not be able to "easily and routinely confirm that a particular enzyme is a thermostable DNA polymerase enzyme."

The response assert that one of skill in the art need not "randomly test" a large number of different amino acid combinations to determine which thermostable enzyme has DNA polymerization and reverse transcription activity. First, MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results,

commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant." Here, the statements regarding the identity of a thermostable DNA polymerase based upon its function and primary-structural similarity must be supported by evidence, not argument. The response has provided no evidence directed to the particular sites and whether these sites may tolerate substitutions to be able to polymerize and reverse transcribe.

The response further asserts that "the lack of complete conservation within the critical motif of the thermostable DNA polymerase does not affect the ability of one of skill in the art to use the full scope of the claimed methods." This argument, like the argument above, has not been supported by evidence. There is no evidence of record that mutations in various positions will maintain the activity of the polymerase. The specification provides examples of position 4 which illustrate that not all of the positions are efficient. Thus, the ordinary artisan would expect variability in other regions of the "critical motif" will effect the efficiency of the reverse transcriptase. It is unpredictable the effects of each of these mutations.

The response asserts that the examiner has based the enablement rejection solely on the breadth of the claimed invention. This argument has been thoroughly reviewed, but is not found persuasive because each of the Wands factors have been addressed. The rejection addressed the quantity of experimentation to test all of the possible variations at the allowed positions, the teachings of the specification and the

art, the presence of working examples, namely the Table illustrating the variation at position 4 and all of the efficiencies, the breadth of the claims.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-4, 8-10, 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Gelfand et al (EP 0 902 035 A2, March 17, 1999).

Gelfand et al. (herein referred to as Gelfand) teaches thermostable DNA polymerases. Gelfand teaches SEQ ID NO: 2, 3, 4, 5, 6, 7, namely SEQ ID NO: 2, 3, 4, 5, 6, 7, respectively of the instant application. Gelfand teaches that the "DNA synthesis reaction" refers to methods of producing copies of DNA including but not limited to PCR, strand displacement amplification, transcription mediated amplification, primer extension and reverse transcription (page 5). Gelfand exemplifies using the enzymes of the invention to efficiently incorporate nucleotides labeled with fluorescein family dye by

means of a primer extension competitions assay (col. 10). Gelfand also teaches that the mutant polymerases may be used in sequencing methods. Gelfand teaches the method of DNA labeling by providing a thermostable DNA polymerase, providing a nucleotide labeled and performing a DNA synthesis reaction. The thermostable DNA polymerases of the invention are more suitable and desirable for use in processes such as DNA sequencing and in vitro synthesis of labeled products than prior art polymerases. Therefore, since Gelfand teaches every limitation of the claimed invention, Gelfand anticipates the instant claims.

Response to Arguments

The response traverses the rejection. The response asserts the patent does not teach of suggest each and every element of the claimed invention, including a template RNA, a primer and a divalent cation. This argument has been reviewed but is not convincing because the words reverse transcription inherently are directed to transcribing an RNA template. By definition, reverse transcription is copying information found in RNA into DNA. Thus, with respect to the reference not teaching a template RNA, this argument is not persuasive. Additionally, the response argues that Claim 1 requires a mixture that comprises a primer. The instant specification states that "all known reverse transcriptases require a primer to synthesize a DNA transcript from an RNA template" (page 1, line 11-12). Thus, by definition, using a primer is an inherent property of reverse transcription. Finally, the response states that the patent has not taught a divalent cation in a reverse transcription reaction. As evidenced by Maniatis, "Molecular Cloning: Lab Manual" divalent cations are an "absolute requirement for

reverse transcriptase activity. Thus, by the patent describing reverse transcription, they are inherently teaching a template of RNA, a primer, a divalent cation at a temperature sufficient to initiate synthesis.

The response asserts that the ordinarily skilled artisan would not recognize that the patents describe a method for reverse transcribing an RNA. This argument has been thoroughly reviewed, but is not found persuasive because the patent specifically includes reverse transcription within the list of means of DNA synthesis. The patent states that the polymerases may be used in DNA synthesis reactions. The DNA synthesis reactions include reverse transcription (col. 7, lines 25-30). Thus, the patent teaches performing reverse transcription with the polymerases of the instant invention as required by the claims.

Thus for the reasons above and those already of record, the rejection is maintained.

6. Claims 1-4, 8-10, 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Gelfand et al (US Pat. 6,346,379, filed September 3, 1998).

Gelfand et al. (herein referred to as Gelfand) teaches thermostable DNA polymerases. Gelfand teaches SEQ ID NO: 2, 3, 4, 5, 6, 7, namely SEQ ID NO: 2, 3, 4, 5, 6, 7, respectively of the instant application. Gelfand teaches that the "DNA synthesis reaction" refers to methods of producing copies of DNA including but not limited to PCR, strand displacement amplification, transcription mediated amplification, primer extension and reverse transcription (col. 7, lines 25-30). Gelfand exemplifies using the enzymes

of the invention to efficiently incorporate nucleotides labeled with fluorescein family dye by means of a primer extension competitions assay (col. 10). Gelfand also teaches that the mutant polymerases may be used in sequencing methods. Gelfand teaches the method of DNA labeling by providing a thermostable DNA polymerase, providing a nucleotide labeled and performing a DNA synthesis reaction. The thermostable DNA polymerases of the invention are more suitable and desirable for use in processes such as DNA sequencing and in vitro synthesis of labeled products than prior art polymerases. Therefore, since Gelfand teaches every limitation of the claimed invention, Gelfand anticipates the instant claims.

Response to Arguments

The response traverses the rejection. The response asserts the patent does not teach of suggest each and every element of the claimed invention, including a template RNA, a primer and a divalent cation. This argument has been reviewed but is not convincing because the words reverse transcription inherently are directed to transcribing an RNA template. By definition, reverse transcription is copying information found in RNA into DNA. Thus, with respect to the reference not teaching a template RNA, this argument is not persuasive. Additionally, the response argues that Claim 1 requires a mixture that comprises a primer. The instant specification states that "all known reverse transcriptases require a primer to synthesize a DNA transcript from an RNA template" (page 1, line 11-12). Thus, by definition, using a primer is an inherent property of reverse transcription. Finally, the response states that the patent has not taught a divalent cation in a reverse transcription reaction. As evidenced by Maniatis,

"Molecular Cloning: Lab Manual" divalent cations are an "absolute requirement for reverse transcriptase activity. Thus, by the patent describing reverse transcription, they are inherently teaching a template of RNA, a primer, a divalent cation at a temperature sufficient to initiate synthesis.

The response asserts that the ordinarily skilled artisan would not recognize that the patents describe a method for reverse transcribing an RNA. This argument has been thoroughly reviewed, but is not found persuasive because the patent specifically includes reverse transcription within the list of means of DNA synthesis. The patent states that the polymerases may be used in DNA synthesis reactions. The DNA synthesis reactions include reverse transcription (col. 7, lines 25-30). Thus, the patent teaches performing reverse transcription with the polymerases of the instant invention as required by the claims.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 11, 13-16, 20-32, 36-44, 48-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gelfand et al (US Pat. 6,346,379, filed September 3, 1998) or

Gelfand et al (EP 0 902 035 A2, March 17, 1999) in view of Kawasaki (PCR Protocols, Chapter 3, pages 21-27, 1990).

Each of the Gelfand et al. (herein referred to as Gelfand) references teaches thermostable DNA polymerases. Gelfand teaches SEQ ID NO: 2, 3, 4, 5, 6, 7, namely SEQ ID NO: 2, 3, 4, 5, 6, 7, respectively of the instant application. Gelfand teaches that the "DNA synthesis reaction" refers to methods of producing copies of DNA including but not limited to PCR, strand displacement amplification, transcription mediated amplification, primer extension and reverse transcription (col. 7, lines 25-30). Gelfand exemplifies using the enzymes of the invention to efficiently incorporate nucleotides labeled with fluorescein family dye by means of a primer extension competitions assay (col. 10). Gelfand also teaches that the mutant polymerases may be used in sequencing methods. Gelfand teaches the method of DNA labeling by providing a thermostable DNA polymerase, providing a nucleotide labeled and performing a DNA synthesis reaction. The thermostable DNA polymerases of the invention are more suitable and desirable for use in processes such as DNA sequencing and in vitro synthesis of labeled products than prior art polymerases.

Gelfand does not specifically teach a method of reverse transcription using magnesium, primers and DNA polymerase.

However, Kawasaki teaches amplification of RNA methods which employ PCR buffer comprising magnesium, namely MgCl2. Kawaski teaches that the "magnesium concentration is also critical, so care should be taken that the addition of reagents does not lower the magnesium molarity" (page 26). Kawaski teaches that "the source and

type of reverse transcriptase do not seem to be of critical importance." Kawasaki teaches incubating the reaction mixture at 23 and 42 degrees. Kawaski teaches performing PCR following the reverse transcriptase reaction.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have used the mutant polymerases taught by Gelfand to be useful in reverse transcription assays using the specific method of Kawasaki. The ordinary artisan would have recognized that the method provided by Kawasaki was a standard method of RNA amplification. Since Kawasaki clearly indicates that the source and type of reverse transcriptase does not appear to be critical, the ordinary artisan would have been motivated to have substituted the mutant DNA polymerases of Gelfand because they have demonstrated increased efficiency.

Response to Arguments

The response traverses the rejection. The response asserts Kawasaki does not teach or suggest reverse transcription using a thermostable DNA polymerase which is very different from mesophillic retroviral reverse transcriptases. This argument has been reviewed but is not convincing because Kawaski teaches that "the source and type of reverse transcriptase do not seem to be of critical importance."

The response asserts that the first reports of reverse transcription catalyzed by thermostable DNA polymerases was inefficient and insensitive. This argument has been thoroughly reviewed, but is not found persuasive because the claims are not drawn to any particular concentration of magnesium. Thus, the prior art does teach the use of magnesium in RT PCR assays and the teachings in the art to use magnesium

and that divalent cations are an absolute requirement for reverse transciptase activity, the ordinary artisan would have included magnesium within the RT-PCR assay as required by the claims.

The response asserts t hat there is no motivation to combine the references to obtain the invention as a whole. This argument has been thoroughly reviewed, but is not found persuasive because the skilled artisan may combine the references for a different reason. There need not be a suggestion that using the DNA polymerases would have increased activity as suggested by the response (page 31).

With all of the statements directed to improved reverse transcription activity, improved reverse transcription activity in the presence of magnesium ions, etc. the response may be arguing that the claims have an unexpected result over the prior art, however, the claims are not limited to the unexpected results provided in the instant specification. Claims 53, 61 are not limited to magnesium. Moreover, Given the tables on page 27, only 5 of the millions of variations have been tested. The reaction efficiencies are increased for both magnesium and manganese. Thus, it is unclear why applicants suggest magnesium is so preferential. Moreover, the claims are not commensurate in scope with the teachings of the specification.

Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

8. No claims allowable.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Bergquist et al (WO 95/14770, June 1995) teaches SEQ ID NO: 14 of the instant application. The polymerase is taught to be useful in RT-PCR assays. The prior art does not specifically teach a polymerase which does not have a E, A, G or P at postion 4 of the amino acid polymerase. The instant claims require such limitations. Thus, the instant claims do not appear to be anticipated by the teachings of Bergquist.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
October 10, 2003

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600